622. *Esters containing Phosphorus. Part XVIII.* Esters of Ethynylphosphonic Acid.*

By B. C. Saunders and P. Simpson.

Dialkyl ethynylphosphonates have been synthesised. By base-catalysed addition to these compounds, ethanol, diethylamine, ethanethiol, and diethyl malonate have been "phosphonovinylated." Other additions to the ethynylphosphonates are described, including the reaction with diazomethane which gave a pyrazol-5-ylphosphonate. The acetylide ion obtained from the ethynylphosphonates reacted with ketones to give substituted 1,3-dioxolan-4-ylidenemethylphosphonates.

In 1960 we reported the synthesis of esters of ethynylphosphonic acid,[1] $CH{:}C{\cdot}PO(OR)_2$. We now give detailed results of our investigations into the synthesis and properties of these esters.

The dimethyl, diethyl, and di-isopropyl esters have been prepared by the "reverse" addition of ethynylmagnesium bromide to a solution of the appropriate dialkyl phosphorochloridate in tetrahydrofuran. Yields were low as these ethynylphosphonates tend to polymerise. Only a few mg. of the dimethyl ester were obtained as it polymerised readily even at 0°. The di-isopropyl ester was much more stable.

We find that the preparation can be greatly improved if a dialkyl phosphorofluoridate is used instead of a phosphorochloridate. First, the necessity for "reverse" addition (*i.e.*, Grignard reagent to chloridate) is obviated as the ester groups of dialkyl phosphorofluoridates are stable to Grignard reagents.[2] Secondly, phosphorofluoridates are less sensitive than phosphorochloridates to moisture and can be more easily stored. Thus the yields are increased; *e.g.*, the chloridate gives 10—20% of di-isopropyl ethynylphosphonate, but yields from the phosphorofluoridate vary from 25% to 35%.

Using the di-isopropyl ester we have investigated the chemistry of these compounds along the lines outlined earlier.[1]

(A) *Additions across the Triple Bond.*—(i) Treatment of di-isopropyl ethynylphosphonate (I) with bromine in ether gave di-isopropyl 1,2-dibromovinylphosphonate (II). Both geometrical isomers were obtained, as indicated by the nuclear magnetic resonance spectrum.

$$\text{(I) } (Pr^iO)_2P(O){\cdot}C{\equiv}CH + Br_2 \longrightarrow (Pr^iO)_2P(O){\cdot}CBr{=}CHBr \text{ (II)}$$

The nuclear magnetic resonance spectra of the substituted vinylphosphonates obtained from ester (I) were used to determine the proportions of *cis*- and *trans*-isomers. It is hoped to publish the detailed information obtained from these spectra and those of other vinylphosphonates later.

(ii) According to the conditions employed, either one or two molecules of ethanol could be added across the triple bond to give, respectively, di-isopropyl 2-ethoxyvinylphosphonate (III) and 2,2-diethoxyethylphosphonate (IV).

$$(Pr^iO)_2P(O){\cdot}C{\equiv}CH + EtOH \xrightarrow{NaOEt} (Pr^iO)_2P(O){\cdot}CH{=}CH{\cdot}OEt \quad \text{(III)}$$

$$(Pr^iO)_2P(O){\cdot}C{\equiv}CH + 2EtOH \xrightarrow{NaOEt} (Pr^iO)_2P(O){\cdot}CH_2{\cdot}CH(OEt)_2 \text{ (IV)}$$

Both compounds, on acid hydrolysis, gave di-isopropoxyphosphinylacetaldehyde (V), characterised as its 2,4-dinitrophenylhydrazone.

$$(Pr^iO)_2P(O){\cdot}CH{=}CH{\cdot}OEt \xrightarrow{H^+} (Pr^iO)_2P(O){\cdot}CH_2{\cdot}CHO \text{ (V)}$$

$$(Pr^iO)_2P(O){\cdot}CH_2{\cdot}CH(OEt)_2 \xrightarrow{H^+} (Pr^iO)_2P(O){\cdot}CH_2{\cdot}CHO \text{ (V)}$$

* Part XVII, *Tetrahedron*, 1958, **4**, 198.

[1] Hunt, Saunders, and Simpson, *Chem. and Ind.*, 1960, 47.

[2] See Part XIX, p. 3464.

Treatment of tri-isopropyl phosphite with chloroacetal at 170° yielded a product whose infrared spectrum was identical with that of a mixture of esters (III) and (IV).

$$(Pr^iO)_2P + Cl{\cdot}CH_2{\cdot}CH(OEt)_2 \longrightarrow (IV) + Pr^iCl \text{ (Arbusov reaction)}$$

$$(IV) \xrightarrow[\text{Heat}]{-EtOH} (III)$$

This mixture, on treatment with Brady's reagent, yielded the 2,4-dinitrophenylhydrazone of di-isopropoxyphosphinylacetaldehyde.

This clearly indicates that the structures assigned to esters (I), (III), and (IV) are correct and illustrates the lability of the " second " molecule of ethanol which added across the triple bond of the ester (I). The acetal (IV) was partly converted into the enol ether (III) by distillation or completely by treatment with sodamide in liquid ammonia.

The enol ether (III) obtained from the ester (I) by addition of ethanol consisted of a mixture of geometrical isomers, as indicated by its nuclear magnetic resonance spectrum.

(iii) The addition of ethanethiol gave di-isopropyl 2-ethylthiovinylphosphonate (VI).

$$(Pr^iO)_2P(O){\cdot}C{\equiv}CH + EtSH \longrightarrow (Pr^iO)_2P(O){\cdot}CH{=}CH{\cdot}SEt \text{ (VI)}$$

A slow reaction took place when the two compounds were mixed. The product was most conveniently obtained by adding the ethynyl compound to an excess of the thiol containing dissolved sodium. The nuclear magnetic resonance spectrum indicated that a mixture of both isomers (VI) was obtained by the latter method.

(iv) The ester (I) reacted readily with diethylamine to give di-isopropyl 2-diethylaminovinylphosphonate (VII). Only the *trans*-isomer was obtained.

$$(Pr^iO)_2P(O){\cdot}C{\equiv}CH + Et_2NH \longrightarrow (Pr^iO)_2P(O){\cdot}CH{=}CH{\cdot}NEt_2 \text{ (VII)}$$

The product (VII) was hydrolysed by acid to di-isopropoxyphosphinylacetaldehyde (V), identified as its 2,4-dinitrophenylhydrazone.

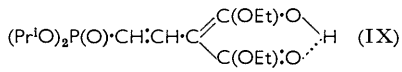
(v) Base-catalysed addition of two molecules of di-isopropyl hydrogen phosphite across the triple bond of the ester (I) readily took place, giving hexaisopropyl ethane-1,1,2-triphosphonate (VIII). This compound gave the expected blue-purple colour with 3,5-dinitrobenzoic acid in 10% aqueous sodium hydroxide.

$$(Pr^iO)_2P(O){\cdot}C{\equiv}CH + 2(Pr^iO)_2PHO \longrightarrow (Pr^iO)_2P(O){\cdot}CH_2{\cdot}CH[P(O)(OPr^i)_2]_2 \text{ (VIII)}$$

(vi) The diethyl malonate anion reacted smoothly with the ester (I) in ethanol to give, after protonation, a compound corresponding to a 1 : 1 adduct. This was an amorphous, pale yellow powder which could not be crystallised and was not, therefore, obtained absolutely pure. The expected reaction was:

$$(Pr^iO)_2P(O){\cdot}C{\equiv}CH + CH_2(CO_2Et)_2 \longrightarrow (Pr^iO)_2P(O){\cdot}CH{=}CH{\cdot}CH(CO_2Et)_2$$

The ultraviolet spectrum of the compound, however, with $\lambda_{max.}$ at 286 mμ and ε 4000, indicated a conjugated system in the molecule of greater length. The infrared spectrum showed an absorption maximum at 1653 cm.$^{-1}$, corresponding to a conjugated carbonyl group which may also be hydrogen bonded, and a doublet at 1583/1550 cm.$^{-1}$, corresponding to a carbon–carbon double bond (or bonds) forming part of a conjugated system longer than that of a substituted vinylphosphonate. This suggested that the product was indeed the expected one, but was completely enolised to give an extended conjugated system (IX) stabilised, probably, by hydrogen bonding.



(IX)

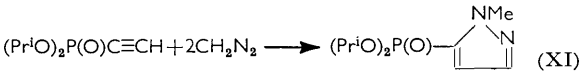
Additional evidence in favour of structure (IX) for this " Michael " adduct is as follows. (*a*) The compound gave a violet colour with ferric chloride in aqueous ethanol. (*b*) Catalytic hydrogenation of the compound gave an undistillable viscous oil, the infrared

spectrum of which contained a normal carbonyl peak at *ca.* 1730 cm.$^{-1}$ and no carbon–carbon double-bond peak. (*c*) Titration with tetramethylammonium hydroxide in dimethylformamide revealed the presence of a weakly acidic hydrogen atom typical of enols.[3] The measured equivalent weight of the compound, obtained from this titration curve, was 360 ± 20. That calculated for structure (IX) is 350. (*d*) The corresponding adduct was prepared from diethyl methylmalonate. This compound (X) has no hydrogen

$$(Pr^iO)_2P(O)\cdot CH{=}CH\cdot CMe(CO_2Et)_2 \quad (X)$$

atom α to the carboxylic ester groups and, hence, cannot enolise. It is a liquid and shows normal carbonyl and carbon–carbon double bond absorptions in the infrared spectrum at 1713 and 1653 cm.$^{-1}$, respectively. Its ultraviolet spectrum, for a neutral solution, was typical of a substituted vinylphosphonate and was unaffected by alkali ($\lambda_{max.}$ 215 mμ; ε 15,600). The ultraviolet absorption of the original adduct was modified by alkali to $\lambda_{max.}$ 298 and 267 mμ (ε 23,600 and 1500, respectively). This derivative (X) from diethyl methylmalonate gave no colour with ferric chloride solution.

(vii) Addition of diazo-compounds to acetylenes is a well-established method for the synthesis of pyrazoles [4-6] and the addition of diazomethane to ethynylphosphonates proved to be a convenient method of synthesising pyrazol-5-ylphosphonates. The ester (I) reacted smoothly with an excess of diazomethane to give di-isopropyl 1-methylpyrazol-5-ylphosphonate (XI) which was hydrolysed with concentrated hydrochloric acid to the free acid (characterised as its anilinium salt). The diazomethane *N*-methylated the pyrazolylphosphonate first formed.



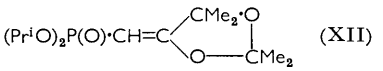
(XI)

Additions (ii), (iii), (iv), and (vi) have been described as " phosphonovinylation."

(B) *Additions to Electrophilic Centres* via *the Carbanion* $(RO)_2P(O)\cdot C{\equiv}C^-$.—(i) In the Zerewitinoff estimation of active hydrogen, carried out on di-isopropyl ethynylphosphonate (I), an almost theoretical amount of hydrocarbon gas was obtained. Attempts to promote reaction between the resulting acetylenic Grignard reagent and various ketones, however, failed. The reaction mixture from such attempts, on hydrolysis, usually returned the ester (I) intact, indicating that the Grignard reagent had not been lost before the desired reaction could take place.

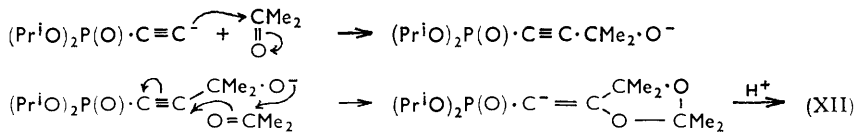
(ii) The use of solid potassium hydroxide suspensions to catalyse the addition of the ester (I) to ketones also failed.

(iii) Treatment of the ester (I) with sodamide in liquid ammonia yielded the carbanion in reactive form. The carbanion readily attacked acetone in a novel way. We have shown the product of this reaction to be the cyclic ketal (XII).



(XII)

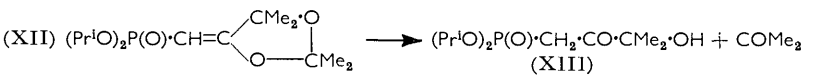
The reaction presumably followed the expected course, but the anion first produced must have attacked a second molecule of acetone to form a cyclic carbanion which, on protonation, yielded the product (XII).

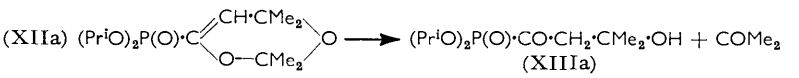


[3] See, *e.g.*, Cundiff and Markunas, *Analyt. Chem.*, 1956, **28**, 792.
[4] Elderfield, " Heterocyclic Compounds," John Wiley and Sons, Inc., New York, 1957, Vol. V, p. 90.
[5] van Alphen, *Rec. Trav. chim.*, 1943, **62**, 485.
[6] Hüttel, Riedl, Martin, and Franke, *Chem. Ber.*, 1960, **93**, 1425.

That the product was a cyclic compound of the type shown, was indicated by its nuclear magnetic resonance spectrum. Apart from the pattern due to the isopropyl ester groups, there was a doublet corresponding to an olefinic hydrogen atom in a position to couple with phosphorus [τ 5·63, J(P/H) 8 c./sec.] and two peaks corresponding to two pairs of methyl groups each in a slightly different chemical environment (τ 8·54 and 8·49) (two methyl groups from the same acetone residue are identical and constitute a pair). The last two peaks showed the methyl groups of the acetone residues to be intact and their singlet nature indicated that there were no other hydrogen atoms attached to the central carbon atoms of the acetone residues.

This gave two possibilities, namely, (XII) and (XIIa). Mild acid hydrolysis yielded one molecule of acetone and one molecule of a hydroxyketo-phosphonate (XIII) whose structure depended upon the structure of the ketal as follows:





The spectroscopic data (nuclear magnetic resonance, infrared, and ultraviolet) favoured (XII) and (XIII). A comparison of the nuclear magnetic resonance spectrum of the hydrolysis product with those of di-isopropyl acetylphosphonate and acetonylphosphonate showed the correctness of structure (XIII) and therefore of (XII). The comparison of the chemical shift and coupling constant to phosphorus of the methylene hydrogen atoms of the product (XIII) with the corresponding figures relating to the acetyl group hydrogen atoms of the acetylphosphonate and the methylene group hydrogen atoms of the acetonylphosphonate is given in the Table.

Compound	Chemical shift (τ)	J(P/H) (c./sec.)
Compound (XIII)	6·69	21
Acetonylphosphonate, >P(O)·CH_2·COMe	6·92	22·6
Acetylphosphonate, >P(O)·COMe	7·6	5·8

The hydrogen atoms referred to are, in the case of compound (XIII) and the acetonylphosphonate, those of the methylene group, and in the acetylphosphonate, those of the methyl group.

Final proof of structure (XIII) and therefore of (XII) was provided by chemical degradation. The carbonyl group of product (XIII) was reduced with sodium borohydride, giving the glycol (XIV):

$$(Pr^iO)_2P(O)\cdot CH_2\cdot CO\cdot CMe_2\cdot OH \longrightarrow (Pr^iO)_2P(O)\cdot CH_2\cdot CH(OH)\cdot CMe_2\cdot OH \quad (XIV)$$

This glycol was then cleaved by sodium periodate and the products (both well known and characterised) were identified by paper chromatography of their 2,4-dinitrophenylhydrazones and the phosphorus-containing compound was isolated and identified by conventional means.

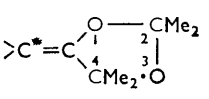
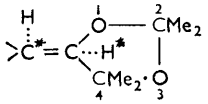
$$(XIV)\ (Pr^iO)_2P(O)\cdot CH_2\cdot CH(OH)\cdot CMe_2\cdot OH \longrightarrow (Pr^iO)_2P(O)\cdot CH_2\cdot CHO + COMe_2$$

Two additional points of interest arise from the stereochemistry of the heterocyclic ring in compound (XII).

(*a*) The nuclear magnetic resonance spectrum of the compound contained only one doublet from an olefinic hydrogen atom. The peak was split by coupling with phosphorus. There was therefore only one such hydrogen atom present and the compound was not a mixture of *cis*- and *trans*-isomers. Dreiding models of the isomers indicated that if the ring-oxygen atom attached directly to the vinyl group were *trans* to phosphorus, then the substituted ring system would interfere with the oxygen groups attached to phosphorus.

No such interference was possible in the other isomer, which would presumably be the only one formed.

(*b*) Secondly, the double bond cannot be catalytically hydrogenated, at any rate at atmospheric pressure. Dreiding models showed that in the unsaturated molecule (XII) the doubly bonded substituent C* and the two 4-methyl groups are in completely staggered conformation. In the hydrogenated molecule (XV), however, the hydrogen atom H*, newly introduced into the ring, and the residue of the doubly bonded substituent C* are now completely eclipsed with respect to the two 4-methyl groups. This presumably

(XII)   (XV)

increases the energy required to hydrogenate the unsaturated molecule, as energy would be required to twist the ring, and it may well explain the failure of the hydrogenation experiments.

(C) *Other Reactions.*—(i) On treatment with alkaline hypobromite,[7] di-isopropyl ethynylphosphonate (I) rapidly yielded the bromoethynylphosphonate $(Pr^iO)_2P(O)\cdot C{\equiv}CBr$. The rapidity of the bromination was fortunate, as alkaline hydrolysis of the ester groups also occurred, but with a reaction period of four minutes yields as high as 74% were obtained.

(ii) In contrast to several other acetylenic phosphorus compounds,[8] the ester (I) was stable to alkali in that the acetylide ion was not displaced by OH^- or by any other base investigated. Triethynylphosphine oxide (obtained by the action of ethynylmagnesium bromide on phosphorus oxychloride) readily yielded acetylene on treatment with dilute aqueous sodium hydroxide.

Strong bases (*e.g.*, the dialkyl phosphite anion or the ethoxide ion) in ether catalysed polymerisation of the ester (I). The latter, in solution in pyridine, slowly polymerised during a period of days.

Probably the only effect of aqueous base on the ethynylphosphonates (apart from ester hydrolysis) is the removal of a proton, to form the acetylide carbanion $(RO)_2P(O)\cdot C{\equiv}C^-$, although this is probably produced only in very low concentration. The ethynylphosphonates give violet colours with 3,5-dinitrobenzoic acid in aqueous alkali, probably by the production of the carbanion.[9]

Experimental

Di-isopropyl Ethynylphosphonate (I).—(*a*) *From di-isopropyl phosphorochloridate.* Ethynylmagnesium bromide was prepared by the method of Jones, Skatteböl, and Whiting [10] from magnesium (4·8 g.) and ethyl bromide (21·8 g.) in dry tetrahydrofuran (170 ml.). It was transferred under nitrogen to a dropping funnel and added during 80 min., under nitrogen, to a stirred solution of di-isopropyl phosphorochloridate (32·1 g.) in tetrahydrofuran (150 ml.). Saturated aqueous ammonium chloride (30 ml.) was then slowly added with stirring. The organic phase was separated and the aqueous phase extracted with tetrahydrofuran (3 × 100 ml.), and dried ($MgSO_4$) overnight, filtered, and further dried ($CaSO_4$). The solvent was removed under reduced pressure and the resultant brown oil distilled at 0·3 mm., to give *di-isopropyl ethynylphosphonate* (6·9 g., 22%). A high bath-temperature was necessary to ensure that the minimum quantity of product remained in the distilling flask. This resulted in superheating of the vapour and the recorded distillation temperature was considerably higher than the b. p. of the product. On redistillation it had b. p. 50—60°/0·1 mm. [Found: C, 49·2; H, 8·3; active H (Zerewitinoff), 0·49%; *M* (matched thermistor method [11]), 181.

[7] Straus, Kolleck, and Heyn, *Chem. Ber.*, 1930, **63**, 1881.
[8] Hartmann, Beerman, and Czempik, *Z. anorg. Chem.*, 1956, **287**, 261.
[9] Saunders and Stark, *Tetrahedron*, 1958, **4**, 197, 198.
[10] Jones, Skatteböl, and Whiting, *J.*, 1956, 4765.
[11] Iyengar, *Rec. Trav. chim.*, 1954, **73**, 789.

$C_8H_{15}O_3P$ requires C, 50·5; H, 7·9; active H, 0·53%; *M*, 190], $\nu_{max.}$ 2075 (C≡C), 3165 (≡CH), and 1263 cm.$^{-1}$ (P=O). The usual phosphonate ester peaks were also present in the spectrum. In the nuclear magnetic resonance spectrum the acetylenic hydrogen atom gave a sharp, well-defined doublet indicating that it was coupled with phosphorus [τ 6·31, J(P/H) 11 c./sec.]

The analytical data and other evidence indicated that the ester always contained a small quantity of an impurity (probably tri-isopropyl phosphate) which could not be removed by fractional distillation. Subsequent use of the recorded b. p. and n_D as criteria for identification should be made, therefore, with caution.

Diethyl ethynylphosphonate, prepared similarly (25%), had b. p. 75—77°/0·1 mm. (Found: C, 44·5; H, 7·3. $C_6H_{11}O_3P$ requires C, 44·45; H, 6·8%).

(*b*) *From di-isopropyl phosphorofluoridate.* Ethynylmagnesium bromide was prepared as in (*a*) from magnesium (9·8 g.) and ethyl bromide (44·4 g.) in dry tetrahydrofuran (450 ml.). Di-isopropyl phosphorofluoridate (52·4 g.) in dry tetrahydrofuran (150 ml.) was added to this under nitrogen and with stirring during 90 min. The mixture was then stirred for 10 min. and saturated ammonium chloride solution (60 ml.) was slowly added with stirring and the whole was cooled in ice–water. Distilled water (200 ml.) was added and the organic phase was removed. The residual aqueous phase was extracted with ether (3 × 100 ml.), and the extracts were combined with the tetrahydrofuran solution. A small quantity of water separated at this stage and was removed. The ether–tetrahydrofuran solution was dried ($MgSO_4$) and evaporated under low pressure. The residual brown tar distilled at *ca.* 0·1 mm., to yield crude di-isopropyl ethynylphosphonate which was shaken for 15—20 min. with 10% aqueous sodium hydroxide to remove traces of the toxic di-isopropyl phosphorofluoridate before distillation. Yields varied from 25 to 35%.

Addition of Bromine to Di-isopropyl Ethynylphosphonate.—To a solution of the ester (I) (2·77 g.) in ether (20 ml.) was added bromine (2 ml.) in ether (20 ml.), and the mixture was stirred intermittently for 5·5 hr., then washed with concentrated sodium thiosulphate solution (20 ml.), dilute sodium thiosulphate solution (20 ml.), and distilled water (4 × 20 ml.), dried ($MgSO_4$), filtered, and evaporated, leaving a yellow oil, *di-isopropyl 1,2-dibromovinylphosphonate* (3·30 g., 65%). This was fractionated on a micro-Vigreux column, to give the pure compound, b. p. 87—98°/0·1 mm., n_D^{21} 1·4939 (Found: C, 28·0; H, 4·7. $C_8H_{15}Br_2O_3P$ requires C, 28·4; H, 4·3%).

Di-isopropyl 2,2-Diethoxyethylphosphonate.—The ester (I) (2·18 g.) was dissolved in a solution of sodium ethoxide (ethanol 60 ml., sodium 0·544 g.). The solution was heated under reflux for 4 hr. and set aside for a further hour. Water (200 ml.) was then added and the mixture extracted with ether (100 ml. + 2 × 50 ml.) and dried ($MgSO_4$). The ether was removed under reduced pressure, leaving a colourless oil, di-isopropyl 2,2-diethoxyethylphosphonate (2·55 g., 79%). This was fractionated at low pressure on a micro-Vigreux column, to give a mixture of di-isopropyl 2,2-diethoxyethylphosphonate and 2-ethoxyvinylphosphonate (Found: C, 50·4; H, 9·9. Calc. for $C_{12}H_{27}O_5P$: C, 51·1; H, 9·65. Calc. for $C_{10}H_{21}O_4P$: C, 50·8; H, 9·0%).

Preparation of Di-isopropyl 2-Ethoxyvinylphosphonate.—The ester (I) (1·82 g.) was treated with sodium ethoxide (ethanol 40 ml., sodium 221 mg.). The resulting solution was set aside at room temperature for 2 hr. Water (40 ml.) was added and the excess of ethanol removed at low pressure. The mixture was extracted with ether, dried ($MgSO_4$), and evaporated under reduced pressure. The residual oil was *di-isopropyl 2-ethoxyvinylphosphonate* (1·94 g., 85%). It was fractionated on a micro-Vigreux column, giving the almost pure compound, b. p. 70—72°/1 × 10^{-3} mm., n_D^{22} 1·4335 (Found: C, 49·9; H, 8·5. $C_{10}H_{21}O_4P$ requires C, 50·8; H, 9·0%).

Arbusov Reaction between Tri-isopropyl Phosphite and Chloroacetal.—Tri-isopropyl phosphite (13·5 g.) and chloroacetal (9·9 g.) were mixed in a flask fitted with a fractionating column and small receiver cooled in ice–salt. The apparatus was designed to allow the volatile alkyl halide, as it was formed, to pass up the column into the receiver, while the reactants and the required product were retained in the reaction vessel. The reaction mixture was maintained at 170° for 35 hr. while isopropyl chloride slowly distilled over. The residual liquid was then fractionated on a 6″ column packed with glass helices, and the fraction of b. p. 88—90°/1 × 10^{-3} mm. was collected. The infrared spectrum of this fraction was identical with that of the mixture of acetal and ethoxyvinylphosphonate obtained from the ester (I).

Acid Hydrolysis of Di-isopropyl Ethynylphosphonate–Ethanol Adducts.—(*a*) The mixture (558 mg.) of acetal and ethoxyvinylphosphonate obtained by distillation of the di-isopropyl

2,2-diethoxyethylphosphonate was heated under reflux for 5 min. with Brady's reagent [12] (8·7 ml.), and the mixture was cooled. The pale yellow needles (656 mg., 66%) that separated were filtered off and recrystallised from aqueous methanol, to give *di-isopropoxyphosphinylacetaldehyde 2,4-dinitrophenylhydrazone*, m. p. 134—135° (the m. p. decreased by several degrees after storage for a number of months) (Found: C, 43·0; H, 5·4; N, 14·5. $C_{14}H_{21}N_4O_7P$ requires C, 43·3; H, 5·5; N, 14·45%).

(*b*) Di-isopropyl 2-ethoxyvinylphosphonate (266 mg.) was similarly treated with Brady's reagent (4·9 ml.); it gave the same 2,4-dinitrophenylhydrazone, m. p. 127—130°, in 80% yield.

Acid Hydrolysis of the Product of Reaction between Tri-isopropyl Phosphite and Chloroacetal.—The liquid ester (247 mg.) was treated with Brady's reagent (3·9 ml.) as above, to give the same crystalline derivative, m. p. 129—130°, in 80% yield.

The products of each of the last three reactions did not have exactly the same m. p. The m. p.s of 2,4-dinitrophenylhydrazones are notoriously unreliable for identification and therefore identity of the three products was proved as follows: (i) Mixed m. p.s. (ii) Chromatography on paper, with Meigh's descending 1 : 1 heptane–methanol system;[13] each gave the same R_F (0·24) in side-by-side tests. (iii) Infrared spectra. (iv) Ultraviolet absorption maxima at 353 and 260 mμ (ε 27,900, 14,200).

Action of Sodamide in Liquid Ammonia on Di-isopropyl 2,2-Diethoxyethylphosphonate.—Sodium (0·4 g., slight excess for 2 g.-atoms per mole of acetal) was dissolved in liquid ammonia (20—30 ml.). Di-isopropyl 2,2-diethoxyethylphosphonate (2·16 g.) [undistilled; free from 2-ethoxyvinylphosphonate; prepared by addition of ethanol to the ester (I)] was added, with stirring, after the blue colour of the sodium solution had been discharged. A brown colour developed at once. The mixture was stirred for 2 hr. under reflux (acetone–carbon dioxide-cooled condenser). Ammonia (*d* 0·88; 4 ml.) was then added, followed by water (7 ml.) and ether (30 ml.). Stirring was continued for 1·5 hr., then the ethereal solution (A) was separated. The aqueous phase was extracted with ether and the extract combined with (A). The ethereal solutions were dried ($MgSO_4$), filtered, and evaporated under reduced pressure. The infrared spectrum of the residual oil was identical with that of di-isopropyl 2-ethoxyvinylphosphonate. The product (1·83 g., 100%) was fractionated, to give the pure compound, b. p. 88—89·5°/3 × 10^{-3} mm., n_D^{22} 1·4335 [cf. b. p. 70—72°/1 × 10^{-3} mm., n_D^{22} 1·4365, for product obtained by addition of one mole of ethanol to the ester (I)].

Di-isopropyl 2-Ethylthiovinylphosphonate.—The ester (I) (2·04 g.) was added slowly, with ice–water cooling, to sodium (0·247 g.) dissolved in ethanethiol (7 ml.) (the reaction between the sodium and the thiol had been allowed to proceed to completion). When the initial vigorous reaction had subsided, the product was set aside for several minutes, water was added, and the mixture was extracted with ether. The ethereal extract was washed with 10% sodium hydroxide solution (3 × 10 ml.) and water (10 ml.) (to remove the excess of thiol). The ether layer was dried ($MgSO_4$) and evaporated under reduced pressure. The residual oil (2·40 g.) was fractionated on a micro-Vigreux column. After 0·59 g. of impurity had distilled, *di-isopropyl 2-ethylthiovinylphosphonate*, b. p. 91—102°, n_D^{15} 1·4830 (1·31 g., 49%), was collected (Found; C, 47·6; H, 8·6. $C_{10}H_{21}O_3PS$ requires C, 47·6; H, 8·4%).

Di-isopropyl 2-Diethylaminovinylphosphonate.—The ester (I) (2·96 g.) was dissolved in an excess of diethylamine, whereupon a spontaneous exothermic reaction took place. The solution was heated under reflux on a water-bath for 30 min., then cooled, and the excess of diethylamine was removed by warming under reduced pressure. The oil (3·36 g., 83%) was fractionated on a micro-Vigreux column fitted with a Fenske return head, to give *di-isopropyl 2-diethylaminovinylphosphonate*, b. p. 114°/0·05 mm., n_D^{20} 1·4649 (Found: C, 54·5; H, 10·6; N, 5·0. $C_{12}H_{26}NO_3P$ requires C, 54·7; H, 9·9; N, 5·3%).

This phosphonate (294 mg.) was heated under reflux in Brady's reagent (4·5 ml.) for 5 min. and then cooled. The product separated as pale yellow needles, m. p. (after recrystallisation from aqueous methanol) 130—132° (339 mg., 85%). By the means outlined above, this compound was shown to be identical with the 2,4-dinitrophenylhydrazone obtained from the ethanol–ester (I) adducts.

Hexaisopropyl Ethane-1,2,2-triphosphonate.—The ester (I) (1·69 g.) was treated with di-isopropyl phosphite (22 g.) in which sodium (0·413 g.) had been dissolved. In order to keep the sodio-phosphite in solution it was necessary to warm the solution slightly before adding it to

[12] Brady, *J.*, 1931, 756.
[13] Meigh, *Nature*, 1952, **170**, 579.

the phosphonate. The solution, which became pale brown at once, was set aside for 40 min. Water was added and the mixture extracted with ether and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue fractionated at 3 mm., to remove the excess of phosphite (15·1 g. recovered, 79%). The remaining viscous oil was distilled at lower pressure, giving *hexaisopropyl ethane-1,1,2-triphosphonate*, b. p. 142°/6 × 10^{-4} mm., n_D^{20} 1·4430 (2·5 g., 54%) [Found: C, 46·2; H, 8·75%; *M* (matched thermistor method [11]), 522. $C_{20}H_{45}O_9P_3$ requires C, 45·8; H, 8·7%; *M*, 522]. Addition of one drop of the compound to a solution of 3,5-dinitrobenzoic acid in 10% aqueous sodium hydroxide gave a purple-violet colour. No colour was observed when the compound was added to 3,5-dinitrobenzoic acid dissolved in 10% aqueous sodium carbonate.

Addition of Diethyl Malonate to the Ester (I).—The phosphonate (I) (2·29 g.) and diethyl malonate (2·30 g.) were mixed and a solution from sodium (0·3 g.) in ethanol (14 ml.) was added with stirring during 12 min. The mixture became pale yellow almost at once, with a slight rise in temperature, and stirring was maintained for 80 min., then water (14 ml.) was slowly added with stirring. The resulting mixture was extracted with ether and dried ($MgSO_4$). After removal of the solvent a very viscous yellow syrup (3·2 g.) remained. This was washed with ether, and then solidified to a pale yellow powder (1·54 g.). This was the principal product, the expected "Michael" adduct (34% yield). It was non-crystalline and had no definite m. p.; it sintered at 124°, became transparent at 151°, and effervesced at 180°. After further trituration with ether, this (impure) enolic diethyl di-isopropoxyphosphinylvinylmalonate was analysed (Found: C, 48·7; H, 7·5. Calc. for $C_{15}H_{27}O_7P$: C, 51·4; H, 7·8%). The molecular weight was determined cryoscopically in dimethyl sulphoxide, and the equivalent weight by potentiometric titration with tetramethylammonium hydroxide in dimethylformamide (the enolic hydroxyl group is acidic) (Found: *M*, 349; Equiv., 340—380. Calc. for $C_{15}H_{27}O_7P$: *M*, 350; Equiv., 350).

Addition of Diethyl Methylmalonate to the Ester (I).—To a stirred mixture of the phosphonate (1·81 g.) and diethyl methylmalonate (1·66 g.) a solution from sodium (0·220 g.) in ethanol (9·5 ml.) was added during 5 min. The solution became yellow immediately with slight rise in temperature. Stirring was continued at room temperature for 1 hr., then water was added. The resultant mixture was extracted with ether, and the extract was dried ($MgSO_4$) and evaporated. The residue was distilled, giving impure diethyl *C*-(di-isopropoxyphosphinylvinyl)-*C*-methylmalonate, b. p. 83°/2 × 10^{-3} mm., n_D^{20} 1·4510 (1·11 g., 32%) [Found: C, 51·5; H, 8·4%; *M* (matched thermistor method [11]), 336. Calc. for $C_{16}H_{29}O_7P$: C, 52·8; H, 8·05%; *M*, 364].

Di-isopropyl 1-Methylpyrazol-5-ylphosphonate.—To the ester (I) (3·15 g.) a large excess of diazomethane in ether [14] (not distilled) was added. The mixture was set aside overnight and the excess of diazomethane and the ether were then removed under reduced pressure. The residual oil was dissolved in ether (30 ml.) and was extracted with concentrated hydrochloric acid. The acid extract was basified with sodium hydroxide solution, diluted, and extracted with ether (3 × 30 ml.). These ethereal extracts were dried ($MgSO_4$), filtered, and evaporated. The residue (2·70 g.) was fractionated on a micro-Vigreux column and *di-isopropyl 1-methylpyrazol-5-ylphosphonate*, b. p. 85—88°/7 × 10^{-4} mm., n_D^{19} 1·4622, was collected (1·14 g., 28%) [Found: C, 49·1; H, 8·3; N, 11·0%; *M* (matched thermistor method), 237, 244. $C_{10}H_{19}N_2O_3P$ requires C, 48·8; H, 8·1; N, 11·4%; *M*, 246].

This product (0·76 g.) was heated under reflux with concentrated hydrochloric acid (6 ml.) for 2 hr. Water and hydrochloric acid were removed under reduced pressure. Last traces of both were removed by reducing the pressure over the resultant clear colourless gum to 2 × 10^{-2} mm. for 15 hr. This resulted in partial crystallisation of the phosphonic acid in needles (0·492 g., theoretical), but a quantity of gum remained. The acid (0·412 g.) was dissolved in ethanol, and aniline added dropwise until no more solid was precipitated. The solid was filtered and dried (0·530 g., 79%). A portion recrystallised from ethanol to give *anilinium 1-methylpyrazol-5-ylphosphonate*, with one mol. of ethanol of crystallisation, m. p. 200—203° (Found: C, 47·8; H, 6·1. $C_{10}H_{14}N_3O_3P,C_2H_6O$ requires C, 47·8; H, 6·6%). Storage over phosphorus pentoxide in a desiccator gave the unsolvated *salt* (Found: C, 47·3; H, 5·9; N, 16·7. $C_{10}H_{14}N_3O_3P$ requires C, 47·1; H, 5·5; N, 16·5%).

Di-isopropyl 2,2,4,4-Tetramethyl-1,3-dioxan-4-ylidenemethylphosphonate (XII).—Sodium (0·73

[14] Vogel, "A Textbook of Practical Organic Chemistry," Longmans, Green and Co., London, 1948, p. 844.

g.) was dissolved in liquid ammonia (*ca.* 50 ml.) and, with stirring, the ester (I) (6·0 g.) was added during 1 min. The blue colour was rapidly discharged. Acetone (2·5 ml.) was then similarly added and stirring was continued for 3 hr. under a carbon dioxide–acetone-cooled condenser. Ammonium chloride (1·7 g.) was added and stirring continued for 5 min. The mixture was set aside overnight while the ammonia evaporated. Water (80 ml.) was then added and the mixture extracted with ether; the extract was dried ($MgSO_4$), filtered, and evaporated by warming it under reduced pressure. The residual brown oil (6·2 g.) was fractionated on a micro-Vigreux column, to give the pale yellow *adduct* (XII), b. p. 115—117°/0·2 mm., n_D^{20} 1·4469 (3·85 g., 40%) [Found: C, 54·5; H, 9·25%; *M* (matched thermistor method), 291. $C_{14}H_{27}O_5P$ requires C, 54·9; H, 8·9%; *M*, 306].

Acid Hydrolysis of the Adduct (XII).—(*a*) *Isolation of the phosphorus-containing fragment.* The adduct (2·51 g.) was dissolved in methanolic sulphuric acid (80 ml.; methanol–concentrated sulphuric acid–water, 15 : 2 : 5) and set aside overnight, then kept at 40° for 1 hr. Water (150 ml.) was added, the mixture was extracted with ether (4 × 50 ml.), and the extracts were dried ($MgSO_4$) and evaporated. The residue (1·48 g., 85%) was distilled, to give *di-isopropyl 3-hydroxy-3-methyl-2-oxobutylphosphonate*, b. p. *ca.* 86°/0·1 mm., n_D^{19} 1·4366 (1·1 g., 63%) [Found: C, 49·8; H, 9·15%; *M* (matched thermistor method), 272. $C_{11}H_{23}O_5P$ requires C, 49·6; H, 8·7%; *M*, 266].

(*b*) *Isolation of phosphorus-free fragment.* The adduct (0·781 g.) was treated with Brady's reagent (16·0 ml., *ca.* 50% excess). After several minutes, crystals separated slowly. The mixture was set aside overnight and the acetone 2,4-dinitrophenylhydrazone (0·5080 g., 0·93 mol.) was filtered off. The filtrate (F) was reserved (see below). After recrystallisation from ethanol, the solid had m. p. and mixed m. p. 125—126°. Paper chromatography in the descending heptane–methanol system [13] also indicated that the compound was acetone 2,4-dinitrophenylhydrazone, R_F 0·5. Water was added to the filtrate (F) and this mixture was then extracted with chloroform. The extract was dried ($MgSO_4$), filtered, and evaporated. The residue (0·786 g.) was distilled at low pressure; the infrared spectrum of the distillate was identical with that of di-isopropyl 3-hydroxy-3,3-dimethylacetonylphosphonate isolated from the hydrolysis previously described.

Reduction of Di-isopropyl 3-Hydroxy-3-methyl-2-oxobutylphosphonate with Sodium Borohydride.—The phosphonate (445 mg.) was dissolved in 95% ethanol (4·3 ml.), and sodium borohydride (24·3 mg.) was added. The mixture was kept at room temperature for 15 min., then warmed to ~50° for 2 min. Water (4·3 ml.) was added and the solution boiled, cooled, diluted with more water, and extracted with ether (6 × 10 ml.). The extracts were dried ($MgSO_4$), filtered, and evaporated at low pressure. The residue (200 mg., 45%) was crude di-isopropyl 2,3-dihydroxy-3-methylbutylphosphonate. The infrared spectrum of this compound showed the characteristic isopropyl phosphonate ester peaks and a very intense hydroxyl peak at 3400 $cm.^{-1}$.

Oxidation of the 2,3-Dihydroxy-3-methylbutylphosphonate with Sodium Periodate.—(*a*) *Identification of the fragments by paper chromatography.* The crude phosphonate (104 mg.) was dissolved in water (2 ml.), and sodium metaperiodate (90 mg.) was added. The solution was shaken and set aside for 90 min. Pouring it into a saturated solution of 2,4-dinitrophenylhydrazine in dilute hydrochloric acid gave a pale yellow oil that was extracted with chloroform and dried ($MgSO_4$). Small quantities of this chloroform solution were applied to paper and solutions of di-isopropoxyphosphinylacetaldehyde 2,4-dinitrophenylhydrazone and acetone 2,4-dinitrophenylhydrazone were applied to the same paper. The chromatogram was developed in Meigh's system; [13] the oxidation products gave two spots corresponding to those of these two controls (R_F 0·20 and 0·42, respectively).

(*b*) *Isolation of the phosphorus-containing fragment.* Crude di-isopropyl 2,3-dihydroxy-3-methylbutylphosphonate (200 mg.) was dissolved in water (4 ml.), and sodium metaperiodate (173 mg.) added. The solution was shaken and set aside for 100 min., then continuously extracted with ether for 5 hr., in the hollow-stirrer type of extraction apparatus. The extract was dried ($MgSO_4$), filtered, and evaporated under reduced pressure, leaving a colourless oil (160 mg.) whose infrared spectrum was identical with that of di-isopropoxyphosphinylacetaldehyde. With Brady's reagent, this gave a 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 132—133° (from aqueous methanol).

Di-isopropyl Bromoethynylphosphonate.—The ester (I) (2·23 g.) was dissolved in light petroleum (40 ml.; b. p. 40—60°) and shaken vigorously for 4 min. with an alkaline solution

of potassium hypobromite (160 ml.) made up as described by Straus, Kolleck, and Heyn.[7] The organic phase was separated and the aqueous phase extracted with light petroleum. The extract was combined with the original organic phase and dried ($MgSO_4$). The solvent was removed under reduced pressure, leaving an oil (2·33 g., 74%) which was fractionated on a micro-Vigreux column, to give *di-isopropyl bromoethynylphosphonate*, b. p. 76—78°/10^{-3} mm., n_D^{20} 1·4651 [Found: C, 36·4; H, 5·5%; *M* (matched thermistor method), 271. $C_8H_{14}BrO_3P$ requires C, 35·7; H, 5·2%; *M*, 269].

Nuclear Magnetic Resonance Spectra.—These were obtained at 40 Mc./sec. by using a Varian Associates V4300B spectrometer and 12″ electromagnet with flux stabilisation and sample spinning. Positions of references are quoted as chemical shifts on the τ scale [$\tau(SiMe_4)$ = 10·00] and have been measured (in the cases of proton resonance) against tetramethylsilane as internal reference, with side-bands generated by a Muirhead-Wigan D695A decade oscillator.

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